

## REMARKS

### Claims

Claims 1–12 are currently under examination with claims 4 and 9 cancelled without prejudice or disclaimer. Claims 13–15 are added by this paper.

### Claim amendments

The claims have been amended to recite US process claims in accordance with conventional US practice. Entry and examination thereof is respectfully submitted.

Amended claim 1 incorporates some of the elements of claim 4, which is now cancelled. Support for the amendment can be found in, for example, the disclosure contained in page 6, line 23 of the originally-filed specification.

The subject matter cancelled from claims 2 and 3 are recited in new claims 13 and 14, respectively.

New claim 15 recites the elements of claims 2 and 3. Support for the new claim can be found in, for example, the discourse contained in the paragraphs bridging page 5, lines 10 and page 6, line 13 of the instant specification and the disclosure contained in the Examples.

It is respectfully submitted that the claim amendments do not raise new matter.

### Specification

Applicants are in the process of preparing a substitute specification. Inasmuch as the objection of the specification is of formal in nature, requiring an amendment of the British English lexicon to American English, the Examiner is cordially requested to hold the objection of the specification in abeyance until a substitute specification is furnished.

### IDS

Copies of the non-patent literature references are enclosed herewith, rendering the objection thereof moot.

### Rejection under 35 U.S.C. §101/§112, ¶2

The Examiner is thanked for his careful review of the claims. The rejections, not specifically discussed herein, are moot in view of the amendments. Withdrawal of the rejection is respectfully requested.

### **Rejection under 35 U.S.C. § 112, ¶1**

Applicants respectfully disagree with the Examiner's contention that the instant specification fails to provide adequate written description of prodrug compounds of the molecules employed herein. For example, based on the express understanding of prodrug molecules and the art-recognized structure of lipoic acid, the skilled worker can use routine techniques (for example, redox chemistry) to synthesize prodrug molecules which are employable in the methods claimed herein. Explicit recitation of such molecules is not necessary. However, in order to facilitate prosecution, the claims have been amended. It is earnestly submitted that the rejection is moot in view of the amendments.

### **Rejection under §102(b)/§103(a)**

The rejection of claim 12 under §102(b) as allegedly anticipated by Keller et al. (US 6,262,019) is respectfully traversed.

It is courteously submitted that insofar as Keller is silent with regard to the method of administration of the claimed molecules as recited in the instant claims, the cited reference cannot anticipate what is claimed herein. For anticipation, the cited reference has to meet each and every element of Applicants' claims. As such, the rejection is moot in view of the amendments. Withdrawal of the rejection is respectfully requested.

### **Obviousness rejection**

The contention that the subject matter of the instant claim 12 is rendered obvious by Engelen (*American Journal of Resp. Crit. Care Med.*, 2000) in view of the aforementioned reference by Keller is respectfully traversed. Applicants further traverse the rejection of claim 12 under the same section as allegedly rendered obvious by Smit (US 6,495,170) in view of Keller or alternately by Valenzuela in view of Keller et al.

In levying the obviousness rejection, the Office Action contends that based on Engelen's disclosure on depleted glutathione levels in emphysema (which the Office Action alleges is a type of chronic obstructive pulmonary disease or COPD) a skilled artisan would have been motivated to employ with Keller's compositions in a manner recited in the claims. The Examiner contends that a combination of the references *prima facie* renders obvious the instantly claimed subject matter. Applicants disagree with these contentions. A similar rationale is presented with respect to a combination of Smit and Keller.

As explicitly stated in §2143 of the MPEP, “to establish a *prima facie* case of obviousness...the prior art reference (or references when combined) must teach or suggest all the claim limitations.” It is respectfully submitted that the cited references, even at their broadest interpretation, fail to teach or suggest all the elements of Applicants’ claims. As such, inasmuch as a *prima facie* case of obviousness has not been established, the rejection based on the cited Engelen and/or Smit references in view of Keller should be withdrawn.

Engeleen generically teaches glutathione (GSH) levels in the skeletal tissues and the muscle, but is absolutely silent with respect to the presence of this compound in the lungs and/or alveolar macrophage tissue. Based on this article, the skilled artisan would be unaware of the effects of modulating glutathione concentration in the instantly claimed tissues, for example, in the treatment of chronically obstructed lung, as recited in the present claims. Additionally, since both Keller and Engeleen are silent with respect to the administration methodology claimed herein, it is respectfully submitted that the references, even at their broadest interpretation, fail to render obvious the claims of the instant application.

Applicants further submit that Smit, which the Office Action relies on as a primary reference, teaches away from the subject matter of the present claims. For example, in col. 2, lines 17–23, Smit expressly states that:

Intraperitoneal administration of silymarin (200 mg/kg) in rats increased the total glutathione content and improved the reduced glutathione/oxidised glutathione ratio in the liver, intestine, and stomach, while levels of kidney, lung, and spleen were not affected (Valenzuela et al., Selectivity of silymarin on the increase of glutathione content in different tissues of the rat, *Planta Medica* 55, 420-2 (1989)). Emphasis added.

On the basis of this disclosure, the skilled worker has no motivation whatsoever to employ the claimed compounds in a manner recited in the present claims. Withdrawal of the rejection is respectfully requested.

Regarding Valenzuela, Applicants submit that the ABSTRACT discloses the use of silybum compounds in the amelioration of glutathione levels in the liver, intestine and stomach. The ABSTRACT expressly teaches that “treatment does not affect the levels of the tripeptides [presumably, silybum compounds] in the kidney, **lung**, and spleen.” (Emphasis added)

Therefore, Valenzuela in combination of Keller also fails to render obvious the claims of

the instant application.

Withdrawal of all the rejections and passage to allowance is cordially requested.

The Commissioner is hereby authorized to charge any fees associated with this response to Deposit Account No. 13-3402.

Respectfully submitted,

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